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The Broad Range of Coronaviruses Co-existing in Chiropteran: Implications for One Health

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ABSTRACT

Bats are a group of mammals that harbor the most significant number of coronaviruses. The aim of present review article was to analyze the broad spectrum of the coronavirus coexisting in Chiropterans hosts. Bats have certain types of cell receptors that allow them to be the potential hosts of a large number of viruses without the presence of any clinical manifestations, and to be a source of contagion infections for other animals and human species. Emphasis can be placed on five coronaviruses, such as Porcine Epidemic Diarrhea Disease, Severe Acute Diarrhea Syndrome, Middle East Respiratory Syndrome, Severe Acute Respiratory Syndrome, and Severe Acute Respiratory Syndrome 2, which have had significant impacts causing epidemic outbreaks in different parts of the world, and generating implications for both human and animal health. In conclusion, recent research indicated the importance of bats as potential hosts of multiple coroaviruses leading to some zoonotic diseases.

Keywords: Bats, Coronaviruses, Cross-species, Evolution, Spillover, Transmission

INTRODUCTION

Bats are a group of mammals that harbor the most significant number of coronaviruses. Coronaviruses are an extensive family of enveloped RNA viruses, having the ability to infect many species of animals and human beings (Bonilla-Aldana et al., 2020a; Bonilla-Aldana et al., 2020b; Bonilla-Aldana et al., 2021). The types of coronaviruses with high pathogenicity include Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV), Middle East Respiratory Syndrome (MERS-CoV), and the most recent one named SARS-CoV-2 (Bonilla-Aldana et al., 2020a; Bonilla-Aldana et al., 2020b; Bonilla-Aldana et al., 2020f). One of the existing hypotheses given by the co-evolutionary history of bats and virus classes is a bat-virus relationship, which allows both to exist in constant equilibrium, managing to survive together (Banerjee et al., 2018; Wong et al., 2019; Basu-Ray et al., 2020). Bats have diversified cell types and receptors. Therefore, the bats can be potential hosts of many viruses, and thus the spread of viruses increases the possibility of transmission (Bonilla-Aldana et al., 2020c; Bonilla-Aldana et al., 2020d).

Interactions among bats with other animal species and humans can be critical factors for the transmission of coronaviruses, leading to devastating pandemics that affect the whole world (Bonilla-Aldana et al., 2020e; Dhama et al., 2020a; Dhama et al., 2020b). A great example of bat-human interactions occurred in China and Vietnam's restaurants and wildlife markets where zoonotic transmission of viruses has occurred (Wong et al., 2019; Huong et al., 2020).

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BIOLOGY OF BATS

Taxonomy

Bats are among the most diverse mammal order, second after rodents, with a complex taxonomy that is still under study because of conflicting phylogenetic relationships in light of new genetic data, especially at lower taxonomy levels (Amador et al., 2018). These mammals from the order Chiroptera with more than 1400 species share the evolutive characteristic of forelimbs adapted as wings. They were traditionally divided into macro and micro Chiroptera, assuming an independent evolution. However, recent DNA sequence data suggested that megabats (Macrochiropetara) originated during the early Eocene, and shared genetic material with microbats (Tsagkogeorga et al., 2013; Solari et al., 2019). The new proposed suborder is Yinpterochiroptera, including Pteropodidae (megabats) and Rhinolophoidae (horseshoe bats and megadermatidae or false vampire bats). The other suborder is Yangochiroptera (also known as Vespertilioniformes), and is composed of most of the microbat families; echolocation and eating habits evolution are one of the characteristics used in this new classification (Teeling et al., 2000; Eick et al., 2005).

The oldest fossil record of the modern bat ancestor is *Onychonycteris finneyi*, which dated back to the early Eocene (approximately 52.5 million years ago, as a part of the Tertiary Period Cenozoic Era) from the Green River Formation of Wyoming, USA. This fossil proves a piece of evidence that bats evolved the ability to fly before echolocation (Simmons et al., 2008). Currently, the order Chiroptera is composed of more than 1400 species, and various species can evolve together with different viruses. Members of both suborders act as reservoirs or susceptible hosts for several zoonotic viruses that are highly pathogenic in humans (Calisher et al., 2006; Moratelli and Calisher, 2015a; Banerjee et al., 2018). Without causing clinical disease in natural or experimental bats, these flying mammals vary widely in size, shape, and mass, with species weighting from two grams (*Craseonycteris thonglongyai*) to even one kilogram (*Acerodon jubatus*). They are distributed in the world on all continents except Antarctica (Banerjee et al., 2018; Wong et al., 2019).

Their biological diversity is as complex as their taxonomy and their feeding habits range from frugivorous (megabats) to insectivorous, carnivorous, and hematophagous in the Yangochiroptera suborder (Solari and Baker, 2007; Banerjee et al., 2018). They are nocturnal mammals, with one or two peaks of activity during the night; they inhabit a variety of ecological sites, including trees, caves, and other human-made structures, such as tunnels, deserted and occupied houses in rural areas. They spend their time in roosts, creating huge colonies like the one in Bracken cave in the United States of America (Moratelli and Calisher, 2015b), which is composed of more than 20 million bats (*Tadarida brasiliensis mexicana*) (Han et al., 2015).

Although sometimes they are considered seasonal animals. Some species have migratory behavior, especially in temperate zones. They are short-distance migrators, which raises concern about the probability of transmission of pathogens by this species (*Pipistrellus* spp, *Tadarida brasiliensis*, *Vespertilio*, and *Nyctalus* spp.). When they are active, bats provide critical services for the ecosystem by regulating crop pests, as pollinators and dispersing seeds (they are vital for the live cycle of Baobab African tree, *Adansonia digitata*), and fertilizing the soil with their excreta, which is rich in nitrogen control of vectors such as mosquitoes. Bats are used in applied immunogenetic research, as healthy aging models. They have been impacted by the White Nose Syndrome (*Pseudogymnoascus destructans)*. It has been suggested that there has been a decline in the bat population caused by this fungal infection. There are millions of pounds of insects that are not eaten and has turned into a burden for agriculture (Kasso and Balakrishnan, 2013).

Besides their intricate relationship with the environment, with repercussions on human well-being, several host pathogens cause disease in humans. Bats can store around 23 families of detected viruses; some are biological agents responsible for the zoonosis in which the coronavirus is found (Banerjee et al., 2018; Wong et al., 2019).

Knowledge about the bat coronaviruses (Bat-CoV) has increased over the past decade. It is estimated that not lees than 3,204 Bat-CoV worldwide exists. It is known now that they are the main ecological drivers of the diversity of coronaviruses and their evolutionary reservoirs (Banerjee et al., 2019). Bats possess adequate traits to host more viruses, whether these are zoonotic, providing them with a long lifespan for their body size and generating the viral persistence of chronic infections (Lacroix et al., 2017; Banerjee et al., 2019; Wong et al., 2019). The decrease in the physiological activity of the animal in a long way can reduce the immune function and viral replication (Lacroix et al., 2017; Banerjee et al., 2019; Wong et al., 2019).

Due to their role as a primary source of emerging infectious diseases worldwide, the study of the zoonosis associated with bats is vital for understanding the dynamics of transmission, prevention, and control of these pathogens (Banerjee et al., 2018). The bats' ability to be the host of hundreds of viruses without manifesting disease is an extensive area of research, and one of the peculiarities is that these mammals act as a source of infectious diseases. As bats are distributed worldwide with a wide diversity of species at multiple habitats, there is a matter of concern and a field for future related research. They are the only mammals that can fly, look for food daily, and migrate seasonally. For example, the Nathusius's bat (*Pipistrellus nathusii*) showed a mean speed of 47 km/day (Hedenström, 2009). Some species can fly over the ocean up to 14 km from the shore (Ahlén et al., 2009). They can facilitate their flight by having hollow bones to reduce body mass (Han et al., 2015; Fleming, 2019).

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Immunology of coronavirus in bats

Bats possess properties that modify their immune function and allow them to be reservoirs and vectors of diseases instead of being clinically infected (Calisher et al., 2006; Allen et al., 2009). It has been observed during the co-evolutionary history of bats and viruses that they have formed a unique host-pathogen relationship. Coronaviruses cause little or no harm to bats and can take months or years to manifest the disease (Schountz, 2014; Banerjee et al., 2018).

One of the existing hypotheses indicates that bats are not infected by the viruses due to the high body temperature during their flight. They mimic the effects of the response to fever, which results from the consumption of ATP which increases mitochondrial activities facilitating host responses. However, by itself, it is not enough to explain how bats can host viruses without signs of disease. Bats' cells are suggested to interfere with viral replication with the constitutive Interferon (IFN) activity, as well as, with active INF-stimulated Genes (ISG). It has also been suggested that bats use Pattern Recognition Receptors (PRRs) as a surveillance system for infectious threats (Schountz, 2014; Flies and Woods, 2019).

The first lines of evidence that associate a pathogen with a host are detecting combined genome fragments that may have circular DNA or linear RNA from one or two fragmented lines, A cell suitable for spreading a virus must be permissive and also be able to carry proper receptors that allow it to bind to an incoming virus. The immunological characteristics presented above are unique in bats, and allow them to be a virus carrier without getting sick (Dobson, 2005; Han et al., 2015). Some types of bats hibernate so their body temperature and metabolic rate are lowered, and immune responses are suppressed to conserve energy during the winter (George et al., 2011). It is believed that one possible mechanism of transmission of viruses from bats is through their saliva and urine, which can contaminate both the soil and fruits. So the contaminated fruits/soil can be ingested by intermediate hosts, including horses, pigs, civets, or non-human primates (Han et al., 2015). The pathogenicity of such viruses for human beings is still unknown, and possible threats need to be determined. Viruses transmitted by bats have been found in different species and geographical distribution, which indicates that they have been expanding the disease (Han et al., 2015). The related example is pandemic coronaviruses for which bats have been identified as a reservoir par excellence since they are ideal for hosting and transporting the virus to intermediate hosts through wet markets or illegal trafficking resulting in endangering human health (Huong et al., 2020).

Coronavirus

Bats have been the natural reservoir of the coronaviruses for many years (Table 1). Bats have been evolved over the years by immune and biological changes. These animals are sociable and live in colonies of at least 500 bats per square foot, facilitating the transmission of viruses from bat to bat (Han et al., 2015; Mackenzie et al., 2016).

Coronaviruses (CoV) are part of an extensive family of *Coronaviridae*, subfamily Coronavirinae and order Nidovirales. They present an envelope, and are made up of the most extended single-stranded RNA chains present in unsegmented positive sense vertebrates, and have the particularity of producing new strains and recombining; this virus has a high capacity to adapt to its host, and has been classified into four different genuses; Alphacoronavirus, Betacoronavirus, Gammacoronavirus, and Deltacoronavirus (Table 1) (Wong et al., 2019; Dos Santos Bezerra et al., 2020). Coronaviruses contain the protein S located on the surface; it will enable the start of infection by recognizing receptors and membrane fusion; it is a critical factor in the host's specificity (Banerjee et al., 2018).

This virus is highly contagious and zoonotic, which indicates that the transmission can occur from a vertebrate animal to a human, and presents great importance to global public health, being associated with multiple outbreaks that remain an unknown phenomenon. Coronaviruses circulate in nature in various animal species. Alpha-coronaviruses (alphaCoV) and beta-coronaviruses (betaCoV) can infect mammals, while gamma-coronaviruses and delta-coronaviruses mainly infect birds (Mollentze and Streicker, 2020; Rodriguez-Morales et al., 2020). These viruses have been detected globally, and alphaCoV and betaCoV have originated from bats in regions such as Asia, Africa, Europe, North and South America, as well as Australasia (Table 2).

The first case of coronavirus originated from bats and transmitted by an intermediate host was called palm civet, *Paguma larvata*, which was registered during 2002-2003 in the province of Guangdong in China. In the year 2012, the Middle East Respiratory Syndrome Coronavirus (MERS- CoV), which originated from bats, manifested itself in Saudi Arabia with dromedary camels (*Camelus dromedarius*) as an intermediate host. In December 2019, an unidentified pathogen emerged in Wuhan, China, causing severe pneumonia, and later in January 2020, a novel coronavirus (nCoV-2019, currently SARS-CoV-2) was described as the cause. Since then, a global emergency has been aroused due to the pandemic caused by SARS-CoV-2 (the current taxonomic name of the new coronavirus). It is supposed that Coronavirus disease 2019 (COVID19) is originated from bats, but the intermediate host is still undefined. Some coronavirus genuses, such as SARS-CoV and several betaCoVs of the subgenus *Merbecovirus*, are known to be closely related to MERS-CoV and have a common reservoir as horseshoe bats (Wong et al., 2019) (Table 2).

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Table 1. Reported Coronaviruses described in bats and other hosts

Coronavirus	Main affected hosts	Intermediate hosts	Natural hosts
Porcine epidemic diarrhea virus	Pigs	Unknown	Bat (*Scotophilus kuhlii*)
Swine acute diarrhea syndrome coronavirus	Pigs	Uknown	Bat (*Rhinolophus* spp.)
Middle East respiratory syndrome coronavirus	Human and other animals	Camels (*Camelus dromedarius*)	Bats (*Taphozous*)
Severe acute respiratory syndrome coronavirus	Human and other animals	Civets and Himalayan pangolin	Bats (*Rhinolophidae*)
Severe acute respiratory syndrome coronavirus 2	Human and other animals	Still unknown, suspected: pangolin	Bats?

?, Bats are still questioned and studied for SARS-CoV-2.

Table 2. Comparison of epidemic coronavirus versus other dangerous zoonotic bat viruses

	CORONAVIRUS*			FILOVIRUS	PARAMYXOVIRUS
Features	**Middle East respiratory syndrome coronavirus**	**Severe acute respiratory syndrome**	**Severe acute respiratory syndrome 2****	**Marburg virus*****	**Nipah virus**
Human functional receptor	Dipeptidyl peptidase 4 (DPP4 or D26	Angiotensin-converting enzyme 2 (ACE2) and CD209L (L-SIGN)	Angiotensin-converting enzyme 2 (ACE2) host transmembrane serine protease TMPRSS2	T cell immunoglobulin mucin domain-1 (TIM-1)	Ephrin B2 (membrane-bound ligand for the EphB class of receptor tyrosine kinases)
Clinical characteristic	Bilateral pneumonia, diarrhoea	Fever, bilateral pneumonia. Long prodrome	Peripheric bilateral pneumonia, anosmia, dysgeusia. Increasing report of neurological syndromes.	Hemorrhagic fever	Encephalitis, acute respiratory infection
Geographical Origen	Saudi Arabia	Guandong, China	Wuhan, China	Africa	Malaysia (1) Bangladesh (2)
Year of apparition	2012 (ended in sporadic cases still reported)	2002 (ended in 2004)	December 2019 (ongoing)	1967	(1) 1998 (2) 2001
Total of cases since apparition	2,494	8,096	178,879,640	587	Approximately 845
Total deaths	858	774	3,875,132	475	>800
CFR	34%	9.6%	2.17%****	24-80%	40-75%
Chiroptera associated reservoirs	*Taphozous perforatus* (Egyptian tomb bat), *Rhinopoma hardwickii* (lesser mouse-tailed bat) and *Pipistrellus kuhlii* (Kuhl's pipistrelle)	Giant horseshoe bat *(Rhinolophus ferrumequinum)*	Horseshoe bats *(Rhinolophus spp.)*	*Rousettus aegyptiacus*	*Pteropus hypomelanus*
Intermediated host	*Camelus dromedaria* (Camels)	*Paguna larvata* (Palm civet)	Pangolins?	(*Cercopithecus aethiops*) African green monkeys***, pigs?	Pigs, horses, goats, sheep, cats and dogs.
Definitive treatment	No	No	No	No	No
Vaccine	No	No	No	No	No

*Other coronaviruses that cause mild disease: HKU1, NL63, OC43, and 229E. **Up to June 22, 2021. ***Includes variants that cause the same disease: *Lake Victoria Marburgvirus* and *Ravn Marburgvirus*. ****High variation according countries.

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Porcine epidemic diarrhea virus

The swine epidemic diarrhea disease caused by the Porcine Epidemic Diarrhea Virus **(**PEDV-CoV) belonging to the *Betacoronavirus*, was identified in England in 1971. It presents digestive symptoms associated with vomiting and diarrhea manifested in adult and young animals as well as a fatal outcome in newborn animals. The contagion occurred through the oronasal and fecal routes through having contact with secretions, fecal material, food, and water contaminated with the virus. Inter-species transmission occurred in the bat-pig relationship. During 2013, the disease remained registered in Asia, Europe, and America because of high losses since its outbreaks in susceptible pigs of all ages, which defines it as contagious (Piñeros and Mogollón Galvis, 2015; Simas et al., 2015; Banerjee et al., 2019) (Table 2).

According to studies in a recombinant CoV, possibly the PEDV could have been originated from the CoV of *Scotophilus kuhlii* (Han et al., 2019). Strains related to the coronavirus were detected in two *Myotis horsfieldii* bats, in Cambodia and Lao's People Democratic Republic, where the great diversity and presence of coronavirus genetically related PEDV strains that infect pigs, and cattle may promote transmission (Lacroix et al., 2017).

In a lineage of bats of the genus *Scotophilus kuhlii* in Guangxi, China, 11 strains related to the virus were identified (Lacroix et al., 2017; Han et al., 2019). Another study found a CoV with a high relation to PEDV-CoV from Brazil in *Tadarida brasiliensis* bats, which had a zoonotic impact on the appearance of new diseases in humans and animal populations (Piñeros and Mogollón Galvis, 2015). Porcine Epidemic Diarrhea Virus (PEDV) can infect kidney cells of specific brown bats (*Eptesicus fuscus).* However, replication in bat cells needs further studies. No clinical cases of PEDV in humans have been reported. However, it has been shown that it may infect embryonic kidney cells (Zhang et al., 2017; Banerjee et al., 2019).

Swine acute diarrhea syndrome coronavirus

The Swine Acute Diarrhea Syndrome (SADS CoV) is caused by a virus classified in the Alphacoronavirus, a type of coronavirus that emerged in 2017 in the Guangdong province, China (Health, 2018; Zhou et al., 2019). This virus causes an enteric disease that led to the death of 24,693 piglets in southern China. Over time, it was believed the virus has been completely eradicated until February 2019. A new outbreak in the east caused the death of 200,000 piglets, and its transmission mechanism has not yet been clarified. The main symptoms of infected animals were severe diarrhea and weight loss. The obtained results of post-mortem analysis were indicative of intestinal lesions (Zhou et al., 2018).

The SADS-CoV can infect bats, mice, hamsters, rats, gerbils, pigs, birds such as chickens, non-human primates, and potentially humans. However, its zoonotic effect is unknown, it was transmitted through the feces of infected animals or its natural reservoirs. In China, three outbreaks of this virus have been reported so far. It was found that horseshoe bats, such as *Rhinolophus sinicus* and *Rhinolophus affinis*, were the main reservoir bats for SARS-CoV *Sarbecovirus*, MERS-CoV *Merbecovirus*, and SADS-CoV *Rhinacovirus* in South East Asia (Wong et al., 2019; Yang et al., 2019). Studies in Guangdong, China, where stool samples of bats species were collected, showed the detection of coronavirus. In a study, authors found 58 positive samples out of 591, examined by the fecal smears and processed using molecular testing, which indicated that the bats of the species *Rhinolophus sinicus*, *Rhinolophus affinis*, and *Rhinolophus rex* were potential reservoirs of this coronavirus (Zhou et al., 2018) (Table 2).

Middle East respiratory syndrome coronavirus

The Middle East Respiratory Syndrome Coronavirus (MERS-CoV) is a linage C, zoonotic, betacoronavirus enveloped with a positive-sense RNA genome. It was isolated from a man's sputum in Jeddah, Saudi Arabia, in 2012 (Zaki et al., 2012). Subsequent cases and clusters of patients that developed a rapidly evolving bilateral pneumonia, respiratory failure, and death have been reported in the Arabian Peninsula. Since September 2012, a total of 2494 cases have been notified with 858 deaths associated with 27 countries. Studies have indicated that this virus had a case fatality rate of 35% (Banerjee et al., 2019).

Complete genome sequence analysis and serological data provided a piece of evidence for transmission from camels to humans. MERS-CoV-specific RNAs and antibodies were also detected in camels (Reusken et al., 2013; Azhar et al., 2014), so far, there are no antiviral effective treatments for limiting any human coronavirus infection. Fortunately, since late 2020, vaccines have become available against SARS-CoV-2 (St John et al., 2015; Abuhammad et al., 2017).

It is known that bats of the genus *Taphozous perforatus* (Egyptian tomb bat), *Rhinopoma hardwickii* (lesser mouse-tailed bat), and *Pipistrellus kuhlii* (Kuhl's pipistrelle) have acted as the natural reservoir of this virus for many years. Other studies claimed that the dromedary hair participated as an intermediary host for the spread of this virus, and its contact with the man (Banerjee et al., 2019; Fan et al., 2019; WHO, 2020c).

Camels are used in the Middle East for entertainment and transportation so that people can become infected through direct contact with infected camels, and they can shed the virus in their respiratory secretions (Azhar et al., 2014). They have also been detected in camel milk, then there is a risk of infection through consumption of unpasteurized camel milk (Reusken et al., 2014; Han et al., 2015).

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The functional receptor of MERS-CoV is Dipeptidyl Peptidase 4 (DPP4 or CD26), which is present on the surface of the human non-ciliated bronchial epithelial cells (Lu et al., 2013). The receptor can also be found on bats' cells (Cui et al., 2013). Even more, there are descriptions of novel bat coronavirus in South China that attach to this receptor; the clinical implications of these results are unknown (Luo et al., 2018). A study reported that the use of the receptor by the MERS-CoV was different from that used by SARS-CoV and by SARS-CoV-2 (ACE2). The MERS-CoV receptor is conserved and can replicate in both bat cells and human cells (Müller et al., 2012; Han et al., 2015) (Table 2).

Severe acute respiratory syndrome coronavirus

The Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV) is a linage b *Betacoronavirus* and the MERS-CoVs (Maganga et al., 2020). It was based in Foshan, province of Guangdong, China in November 2002 (Fan et al., 2019). The index case was a medical doctor from the province of Guandong who made a trip to Hong Kong Special Administrative Region of the People's Republic of China, five days after the onset of symptoms. After that secondary cases appeared in the city and Singapore, Thailand, Vietnam, and Canada. All the index cases were from those countries where travelers returned from Hong Kong (Tsang et al., 2003). From the first cases, a novel coronavirus was isolated (Drosten et al., 2003). Following that it reached 33 countries and 5 continents, including North America and Europe, causing a global pandemic that lasted eight months, and led to 8096 cases with 774 deaths, reaching a case-fatality rate of 9.6%. The transmission occurred through respiratory drops, micro saliva, or direct contact with the mucous membranes of patients. Extraordinary efforts were made to contain these emerging conditions were deployed globally, including travel advisories by the World Health Organization (WHO) that in consequence led to the end of the epidemic in the first half of 2004 (Vaqué Rafart, 2005).

The SARS is presented as the first epidemic disease of the twenty-first century. It is known that its origin was the wet markets of Guandong, China, where the interaction with fluids and blood of different animals facilitated the propagation. Some studies indicated that the Himalayan palm civet and the palm civet o masked palm civet *(Paguna larvata)* were the intermediaries of this virus as a reservoir host as same as the giant horseshoe bat (*Rhinolophus ferrumequinum*) (Wang et al., 2006; Cleri et al., 2010).

The SARS-CoV produced unusual pneumonia because it had a prolonged prodrome with influenza-like symptoms. The patients develop the respiratory phase with progressive pulmonary infiltrates and respiratory failure. From early in the research, the virus has efficiently replicated *in vitro* (Sims et al., 2008). The functional receptors for SARS-CoV are Angiotensin-converting enzyme 2 (ACE2) and CD209L (L-SIGN) (Jeffers et al., 2004).

The SARS-CoV's genetic components circulated among the various bats' species that share the same cave and the opportunity for a new resurgence (Banerjee et al., 2019; Wong et al., 2019). The SARS virus survives for at least two to four days in feces, and two to three days on dry surfaces at room temperature (Rabenau et al., 2005). The transmission from person to person by direct or indirect contact of the mucous membranes with drops was the primary mode of spread of the pandemic produced in health centers, workplaces, homes, public transport, and air travel; the latter facilitated its rapid worldwide diffusion (Seto et al., 2003; Cheng et al., 2007). The SARS-CoV was detected in feces, urine, and respiratory secretions (Chan et al., 2004). Intra-hospital transmission of the virus was facilitated by nebulizers, intubation, or cardiopulmonary resuscitation in patients with SARS generated by many infectious droplets (Lee et al., 2003; Christian et al., 2004; Loon et al., 2004).

Regarding phylogenetic and viral diversity analyses, studies conducted in Africa, Asia, and Latin America (Peru, Bolivia, Brazil, and Mexico) indicated that intra-genus transmission of bats was higher in Africa and Asia (Health, 2018). The study was also able to confirm that the abundance of the virus was related to many bats (Health, 2018).

A study of an in-hospital outbreak at a community hospital in Toronto on February 23, 2003, indicated that cases of this virus had the age range from 21 months to 86 years, 60.2% of whom were women, and total death of 17 cases. Of the cases identified, 36.7% were hospital personnel. Other cases were locally transmitted or linked to imported SARS cases from other places (29.6%), hospitalized patients (14.1%), visitors (14.1%), or other health staff (5.5%). Of a total of 128 cases, 120 (93.8%) had contact with a SARS-positive case or a place where there was a known case of infection (Varia et al., 2003) (Table 2).

It is essential to know that bats and their products are used in food markets, and as traditional medicine, the feces of bats are used in the south from China and Asia, and consequently, it provides a constant human exposure source to bats and their tissues (Bonilla-Aldana et al., 2020e; Dhama et al., 2020a; Dhama et al., 2020b).

Severe acute respiratory syndrome coronavirus 2

Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), the etiological agent of COVID-19, belongs to the subgenus's genus Betacoronavirus *Sarbecovirus (*same subgenus for SARS-CoV*)*. It has affected the world since January 2020, affecting 210 countries and territories. In December 2019, a cluster of pneumonia with epidemiological nexus with an open-air-live animal market in Wuhan, China, was reported. A novel coronavirus was isolated and named SARS-CoV-2 by the International Committee on Taxonomy Viruses (ICTV). As of June 22, 2021, it has left a balance of

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178,879,640 confirmed cases and 3,875,132 deaths worldwide, but these figures continued to increase (Alanagreh et al., 2020; WHO, 2020a; Tiwari et al., 2020), fortunately 2.76 billion doses of vaccine have been administered. The outbreak was discovered in the Wuhan market, verifying that all the samples obtained from the animals were positive for SARS-CoV-2. This virus had been circulating since November, 2019. On December 1, 2019, the first registered case was found in an elderly man (Mackenzie and Smith, 2020; Yu et al., 2020). Subsequently, significant attempts have been rendered to detect the reservoirs and intermediate host of this emerging infectious disease.

Comparisons revealed that the bat CoV is approximately 79% similar to SARS-CoV at the nucleotide level. Although the MERS and SARS viruses are related to SARS-CoV-2, they have very notable biological differences. SARS-CoV 2 is much more infectious and has a remarkable capacity for local and global spread. It has been taken as a priority to determine the virological characteristics related to transmission. The respiratory pathogen has a relatively high virulence that can jump the barrier species (Chinazzi et al., 2020; Zhang and Holmes, 2020). The bats' role as a zoonotic origin is unknown. The viruses present an association with SARS-CoV-2 were sampled in Yunnan province more than 1,500 km from Wuhan (Wrapp et al., 2020). In a recent publication, a bat coronavirus, RaTG13, was found in *Rhinolophus affinis*, showed 96% genomic similarity to SARS-CoV-2. However, it does not bind efficiently to the human receptor ACE2 (Leitner and Kumar, 2020).

The bat is reported as the reservoir source, but it needs an intermediate host for SARS-CoV-2 to infect humans. A conducted study showed that SARS-CoV-2 replicates poorly in pigs, chickens, and ducks (Flores-Alanis et al., 2020). The pangolins (Pholidota) have been studied as a relevant intermediate host for SARS-CoV-2, with genetic analysis of pangolin CoV, MP789, showing similarities in receptor domains, suggesting an ancestral jump among bats (Flores-Alanis et al., 2020), humans, and pangolins (Fischer et al., 2020; Xiao et al., 2020; Zhang et al., 2020). However, if bats are susceptible to contracting the virus, ferrets, canids, and cats are still possible to directly infect humans (Damas et al., 2020; Leitner and Kumar, 2020; Tiwari et al., 2020). Researchers have proposed the potential risk of reverse zoonotic transmission to bats (anthropozoonosis), because of the magnitude of this historic pandemic and the intricate relationship of SARS-CoV-2 and Chiroptera. Researchers have proposed the potential risk of reverse zoonotic transmission from humans to bats (anthropozoonosis) of the SARS-CoV-2 (Franklin and Bevins, 2020; Olival et al., 2020).

The infection can be acquired by inhaling droplets that can spread from one to two, or by touching contaminated surfaces which can remain viable for several days with favorable atmospheric conditions. However, the viruses are destroyed with hypochlorite sodium products, hydrogen, peroxide, among other substances. The virus is also present in feces and contamination of the water supply leading to the transmission through the oral route (Chen et al., 2020; WHO, 2020b; Kampf et al., 2020).

All people are theoretically susceptible; the large droplets come from the coughs and sneezes of symptomatic or asymptomatic patients before the clinical signs appear, causing severe respiratory diseases such as pulmonary failure and pneumonia. However, the severity of COVID19 is unusually selective, rises with age and coexisting health conditions, including, chronic kidney disease, diabetes mellitus, obesity, smoking, and hypertension. There is also increasing evidence about ethnicity and income for the susceptibility of infection and poorer prognosis (de Lusignan et al., 2020). Human genetic factors, such as polymorphism of the host transmembrane serine protease (TMPRSS2) and ACE2 receptor have been proposed (Hou et al., 2020). Post-placental transmission in women has not yet been clearly described. Studies have shown that higher viral loads are found in the nasal cavity than the throat, without differentiating between symptomatic and asymptomatic people. Patients can infect other humans for as long as symptoms last and even after clinical recovery (Rothe et al., 2020; Singhal, 2020; Zou et al., 2020) (Table 2).

CONCLUSIONS

Bats are potential reservoirs of many viruses, including coronaviruses, but direct transmission to humans has not been demonstrated so far since it requires an intermediate host (Joffrin et al., 2020). Recently, in Peru, the complete genome sequence of an Alphacoronavirus isolated from vampire bats (*Desmodus rotundus*, family Phyllostomidae) from the Amazonas region was reported (Bergner et al., 2020).

Research of coronavirus in bats have become an urgent problem, so it is essential to be able to detect early warning signs, and minimize the subsequent outbreaks given by them in places like Egypt, Oman, Qatar, Saudi Arabia, the Middle East, Africa, and South Asia, have found camelids with the virus mentioned above, which their human-animal transmission can be generated by direct or indirect contact with infected animals (Banerjee et al., 2019; Fan et al., 2019; WHO, 2020c). More research is needed to clarify and understand the susceptibility of infection and variable outcomes.

However, there are still some questions that are left unanswered which necessitates the need for more deep studies addressing the effect of coronaviruses on animals and humans. In 2019, a coronavirus mutation from previous years was presented, and people would be exposed to a higher risk of new pandemics caused by CoVs. Thus, it is equally important to know which intermediate hosts are the means of transmission of bats to human beings.

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DECLARATIONS

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Authors' Contributions

DKBA and AJRM conceived the review, developed the preliminary search strategy, and drafted the manuscript. SDJD, CTO, PJS, VGM, and JLBA refined the search strategy by conducting iterative database queries and incorporating new search terms. SDJD, CTO, PJS, VGM, and JLBA searched and collected the articles. AJRM and DKBA conducted the quality assessment. All authors have critically reviewed this manuscript for relevant intellectual contributions. All the authors read and approved the final submitted version of the paper.

Conflicts of interest

All authors report no potential conflicts.

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